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403/10, 410/10, 413/10, 401/06, A61K 31/5025, 31/505CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
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European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,  
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent  
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## Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,

[Continued on next page]

A1

(54) Title: QUINAZOLINES AS MMP-13 INHIBITORS

WO 02/064572 A1

(57) Abstract: A compound selected from those of formula (I): in which: R<sub>1</sub> represents a group selected from hydrogen, amino, alkyl, alkenyl, aminoalkyl, aryl, arylalkyl, heterocycle, and cycloalkylalkyl, optionally substituted, W represents oxygen, sulphur, or =N-R', in which R' is as defined in the description, X<sub>1</sub>, X<sub>2</sub> and X<sub>3</sub> represent nitrogen or -C-R<sub>6</sub> in which R<sub>6</sub> is as defined in the description, Y represents oxygen, sulphur, -NH, or -N(C<sub>1</sub>-C<sub>6</sub>)alkyl, Z represents oxygen, sulphur, -NR<sub>7</sub> in which R<sub>7</sub> is as defined in the description, and optionally carbon atom, n is an integer from 1 to 8 inclusive, Z<sub>1</sub> represents -CR<sub>8</sub>R<sub>9</sub> wherein R<sub>8</sub> and R<sub>9</sub> are as defined in the description, A represents aromatic or non-aromatic, heterocyclic or non-heterocyclic ring system, m is an integer from 0 to 7 inclusive, the group(s) R<sub>2</sub> is (are) as defined in the description, R<sub>3</sub> represents hydrogen, alkyl, alkenyl, alkynyl, or a group of formula: in which Z<sub>2</sub>, B, R<sub>5</sub>, P and q are as defined in the description, optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof, and medicinal products containing the same are useful as specific inhibitors of type-13 matrix metalloprotease.

**INTERNATIONAL SEARCH REPORT**

In Application No  
PCT/EP 02/01979

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07D239/96 C07D401/12 C07D405/12 C07D409/12 C07D405/14 C07D409/14 C07D471/04 C07D403/12 C07D403/10 C07D401/10 C07D413/10 C07D401/06 A61K31/5025 A61K31/505																	
According to International Patent Classification (IPC) or to both national classification and IPC																	
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D A61K																	
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched																	
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) WPI Data, PAJ, BEILSTEIN Data, EPO-Internal, CHEM ABS Data																	
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left; padding: 2px;">Category *</th> <th style="text-align: left; padding: 2px;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="text-align: left; padding: 2px;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td style="padding: 2px;">X</td> <td style="padding: 2px;">LIVERTON N J ET AL: "Nonpeptide glycoprotein IIb/IIIa inhibitors: substituted quinazolininediones and quinazolinones as potent fibrinogen receptor antagonists" BIOORGANIC &amp; MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 5, 3 March 1998 (1998-03-03), pages 483-486, XP004136889 ISSN: 0960-894X see compound 7 page 481</td> <td style="padding: 2px;">17,18</td> </tr> <tr> <td style="padding: 2px;">X</td> <td style="padding: 2px;">H OGAWA ET AL: "Studies on positive inotropic agents V" CHEM PHARM BULL, vol. 36, no. 6, 1988, pages 2253-2258, XP001080174 see compound X chart I</td> <td style="padding: 2px;">17,18</td> </tr> <tr> <td colspan="3" style="text-align: center; padding: 2px;">-/-</td> </tr> </tbody> </table>						Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	LIVERTON N J ET AL: "Nonpeptide glycoprotein IIb/IIIa inhibitors: substituted quinazolininediones and quinazolinones as potent fibrinogen receptor antagonists" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 5, 3 March 1998 (1998-03-03), pages 483-486, XP004136889 ISSN: 0960-894X see compound 7 page 481	17,18	X	H OGAWA ET AL: "Studies on positive inotropic agents V" CHEM PHARM BULL, vol. 36, no. 6, 1988, pages 2253-2258, XP001080174 see compound X chart I	17,18	-/-		
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-/-																	
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.			<input checked="" type="checkbox"/> Patent family members are listed in annex.														
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Date of the actual completion of the International search		Date of mailing of the International search report															
4 June 2002		25/06/2002															
Name and mailing address of the ISA			Authorized officer														
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016			Scruton-Evans, I														

## INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/EP 02/01979

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 // (C07D471/04, 239:00, 221:00)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>DATABASE CHEMCATS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002201020 ORDER NO A1240/0056923 &amp; "SCREENING COLLECTION" 28 March 2000 (2000-03-28), ZELINSKY INSTITUTE OF ORGANIC CHEMISTRY, 47 LENINSKY PROSPECT, MOSCOW, 117913 RUSSIA</p> <p style="text-align: center;">-/-</p>	1

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- \*P\* document published prior to the International filing date but later than the priority date claimed

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\*&\* document member of the same patent family

Date of the actual completion of the International search

4 June 2002

Date of mailing of the International search report

Name and mailing address of the ISA

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